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10/601,277	06/20/2003	George E. Barringer JR.	3551.1002-000	6447

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HAMILTON, BROOK, SMITH & REYNOLDS, P.C.
530 VIRGINIA ROAD
P.O. BOX 9133
CONCORD, MA 01742-9133

EXAMINER

RAMILLANO, LORE JANET

ART UNIT

PAPER NUMBER

1797

MAIL DATE

DELIVERY MODE

11/28/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/601,277

Applicant(s)

BARRINGER, GEORGE E.

Examiner

LORE RAMILLANO

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 7/23/08.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 22-43, 50-55, 68 and 69 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 22-43, 50-55, and 68-69 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 4/23/04 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 9/29/08
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Status of Claims

1. In applicant's reply filed on 7/23/08, applicant amended claims 22, 33, 34, 50, 54, and 68-69. Claims 22-43, 50-55, and 68-69 are pending and under examination.

Response to Amendment

Prior art rejections

2. The rejections over the prior art over are maintained.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. **Claims 50-54 and 69** are rejected under 35 U.S.C. 102(e) as being anticipated by Burshteyn et al. ("Burshteyn," US Pub. No. 2002/0123154).

Burshteyn teaches a method for preparing a macromolecule sample, comprising: automatically acquiring a liquid mixture, the mixture comprising a macromolecule, one or more rough components that are larger than the macromolecule, and one or more fine components that are smaller than the macromolecule; automatically separating from the macromolecule at least a

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portion of the components by applying the mixture to each of a plurality of filters, with a pressure differential across each filter (i.e. [0009]-[0015], [0054]); and directing a liquid through a filter in a direction opposite to the direction of filtration, the macromolecule thus being directed further in the apparatus for analysis (i.e. [0085]).

Burshteyn further teaches the following: a macromolecule that has a molecular weight between about 1,000 and about 200,000 AMU (i.e. [0035]); fine components comprising salt components (i.e. [0038]); automatically reducing the concentration of the salt components by at least 50% (i.e. [0013]-[0015]); automatically increasing the macromolecule concentration by at least 100% (i.e. [0013]-[0015]); automatically reducing the concentration of the salt components by at least 50% (i.e. [0013]-[0015]); automatically reducing the concentration of the salt components by at least 75% (i.e. [0013]-[0015]); automatically increasing the macromolecule concentration by at least 200% (i.e. [0013]-[0015]); automatically controlling the concentration of ions in the mixture by sensing the ion concentration and adding an ion buffer (i.e. [0059]); and automatically directing a desalination buffer (i.e. 49, fig. 1, [0045]) through the fine filter into the mixture.

Burshteyn further teaches automatically lysing the cells in the liquid mixture by adding a lysis buffer to the cells (i.e. [0051]); selecting the fine filter to separate fine components that have a molecular weight less than about 90% of the molecular weight of the macromolecule (i.e. p. 18, claim 30(a)); automatically combining the macromolecule with a denaturation agent (i.e. [0048]); and

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separating the macromolecule from at least a portion of insoluble lysed cell fragments by automatically applying the mixture to a lysis filter with a pressure differential across the filter (i.e. [0039]).

Claim Rejections - 35 USC § 103

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. **Claims 22-31, 32-35, 41-43, and 68** are rejected under 35 U.S.C. 103(a) as being unpatentable over Burshteyn in view of Sparks.

The teachings of Burshteyn are indicated above.

As to claim 22, while Burshteyn teachings having a plurality of filters, Burshteyn does not specifically teach having a rough filter selected to separate at least a portion of the rough components and a fine filter selected to separate at least a portion of the fine components.

Sparks teaches in FIGS. 3 and 4, an uppermost substrate (12) that is preferably micromachined to have vias (14) sized to filter relatively large cells or particles, e.g., leukocytes, while the middle and lowermost substrates (12) of FIG. 3 and the lowermost substrate (12) of FIG. 4 are micromachined to have vias (14) sized to filter relatively smaller cells or particles, e.g., erythrocytes (i.e. col. 4, lines 52-60). It would have been obvious to a person of ordinary skill in the art to modify Burshteyn's method by having a fine filter and a rough filter because Burshteyn recognizes the advantage of having a plurality of filters and it would be desirable to have a single system comprising multiple filters of different

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sizes to allow the system to perform multiple analysis steps, such as quantitatively analyzing the cells and/or particles in a fluid.

Furthermore, while Burshteyn teaches directing a liquid through a filter in a direction opposite to the direction of filtration, the macromolecule thus being directed further in the apparatus for analysis, Burshteyn does not specifically teach directing this liquid in an opposite direction for cleaning the filter membrane surface to restore the filter membrane characteristics and capacity to its initial state prior to separating the macromolecule. Sparks teaches an automatic back-flushing operation that can be performed to remove cells/particles that have collected at the upstream surface (16) (col. 6, lines 9-15). It would have been obvious to a person of ordinary skill in the art to modify Burshteyn's method by back-flushing the rough filter to clean the filter membrane surface to restore the filter membrane characteristics and capacity to its initial state prior to separating the macromolecule because it would insure that a continuous flow of the fluid sample is being analyzed and prevent the filters from being clogged.

As to claims 32-34, Burshteyn in view of Sparks does not specifically teach controlling the concentration of hydrogen ion to be in a pH range from 6 to 8. It would have been obvious to a person of ordinary skill in the art to modify Burshteyn in view of Sparks by adding a sufficient amount of buffer to the mixture in order to have a pH in the range from 6 to 8 since keeping the blood sample at a neutral pH range will minimize components of the blood sample from degrading.

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Furthermore, Burshteyn in view of Sparks does not specifically teach selecting the rough filter to separate rough components that have a molecular weight greater than about 110% of the molecular weight of the macromolecule. It would have been obvious to a person of ordinary skill in the art to modify Burshteyn in view of Sparks to have a filter that separates rough components that have a molecular weight greater than about 110% of the molecular weight of the macromolecule because it would be desirable to have an additional means for removing the undesirable cellular components from the blood mixture.

7. **Claim 36** is rejected under 35 U.S.C. 103(a) as being unpatentable over Burshteyn in view of Sparks, as applied to claims 22-31, 32-35, 41-43, and 68 above, and further in view of Holmes (US 4830969).

The teachings of Burshteyn and Sparks are indicated above. Burshteyn in view of Sparks does not specifically teach utilizing sodium dodecyl sulfate as a denaturation agent.

Holmes teaches a process comprising heating cellular materials in a solution of lysing agent to lyse the desired cells and to agglomerate water soluble nitrogen containing compounds (abstract). Holmes further teaches utilizing sodium dodecyl sulfate as a denaturation agent (i.e. column 5, lines 38-54). It would have been obvious to a person of ordinary skill in the art to modify Burshteyn in view of Sparks by specifically utilizing sodium dodecyl sulfate as a denaturation agent because it is well known type of agent used for isolating, for example, nucleic acids from biological samples.

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8. **Claims 37-40** are rejected under 35 U.S.C. 103(a) as being unpatentable over Burshteyn in view of Sparks, as applied to claims 22-31, 32-35, 41-43, and 68 above, and further in view of Schnipelsky et al. ("Schnipelsky," US 6645758).

The teachings of Burshteyn and Sparks are indicated above. Burshteyn in view of Sparks does not specifically teach heating the macromolecule between from 70 degrees Celsius to about 100 degrees Celsius for about 60 to about 600 seconds.

Schnipelsky teaches a DNA extraction protocol comprising: denaturing a sample by utilizing surfactants and heating a macromolecule between from 70 degrees Celsius to about 100 degrees Celsius for about 60 to about 600 seconds (i.e. column 17, lines 23-38). It would have been obvious to a person of ordinary skill in the art to modify Burshteyn in view of Sparks by incorporating a heating step, as taught by Schnipelsky, because heating samples to denature cellular components is a well known and commonly used technique that involves minimal costs.

9. **Claim 55** is rejected under 35 U.S.C. 103(a) as being unpatentable over Burshteyn in view of Schnipelsky et al. ("Schnipelsky," US 6645758).

The teachings of Burshteyn are indicated above. Burshteyn does not specifically teach heating the macromolecule. Schnipelsky teaches a DNA extraction protocol comprising: denaturing a sample by utilizing surfactants and heating a macromolecule between from 70 degrees Celsius to about 100 degrees Celsius for about 60 to about 600 seconds (i.e. column 17, lines 23-38).

It would have been obvious to a person of ordinary skill in the art to modify Burshteyn by incorporating a heating step, as taught by Schnipelsky, because heating samples to denature cellular components is a well known and commonly used technique that involves minimal costs.

Response to Arguments

10. Applicant's arguments, filed 7/23/08, have been fully considered but they are not persuasive.

In response to applicant's argument that Burshteyn does not teach "directing a liquid through a filter in a direction opposite to the direction of filtration," examiner respectfully disagrees. It appears that applicant's argument, on p. 10, is focused on one of the embodiments disclosed by Burshteyn (i.e. fig. 3 of Burshteyn). Applicant should note that a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. In paragraphs [0080]-[0085], it appears that Burshteyn properly reads on the claim language at issue, "directing a liquid through a filter in a direction opposite to the direction of filtration," because Burshteyn teaches, in [0082], utilizing a vacuum force to filter the sample, then in [0085], the sample is caused to move in an opposite direction that was applied in [0082], which would read on the recited language, "directing a liquid through a filter in a direction opposite to the direction of filtration."

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce

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the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the Office takes the position that there is motivation to combine Burshteyn and Sparks, for the reasons stated in the prior Office action, filed on 4/18/08. Furthermore, these motivation statements appear to be sufficient evidence to support an obviousness rejection.

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LORE RAMILLANO whose telephone number is (571)272-7420. The examiner can normally be reached on Mon. to Fri.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jill Warden/
Supervisory Patent Examiner, Art Unit 1797

Lore Ramillano
Examiner
Art Unit 1797